11/17/2022 “One In A Million – Seeking A Cure For Chordoma”

The title of my talk today is “One in a Million – Seeking a Cure For Chordoma.

I have a question for you – is there anyone in this room who hasn’t known someone with cancer?

In today’s world, unfortunately, most of us have known someone with some form of cancer…it could be breast cancer, pancreatic cancer, lung cancer, prostate cancer, or other kinds of cancer.

I am here today to tell you about a very ultra-rare cancer called Chordoma; to share some of my experience with this cancer; to explain the complications to finding a cure; and then tell you what is being done to find a cure and why there is hope for the future.

Tonight, as I give my presentation, I am asking for your participation in a small, but important way – as I reach the end of each page of my notes, I am going to ask you to take turns in honoring someone special in your life who has or had some form of cancer by saying their name. They can be living or passed away. If you’re not comfortable saying their name, you could just mention their relationship to you, such as cousin or friend. You don’t have to say anything if you prefer not to. The person I am honoring tonight is my husband, Marty.

The problem –

A chordoma is a rare type of cancerous tumor that can occur anywhere along the spine, from the base of the skull (cervical) down to the thoracic (upper back), lumbar area (mid to lower back) and then down to the sacral area (the tailbone.) Chordomas grow slowly, gradually extending into the bone and soft tissue around them. Delayed diagnosis and initial misdiagnosis are common.

It is complicated to treat due to the involvement of critical structures such as the brainstem, spinal cord, and important nerves and arteries. Local recurrence is common; many patients experience more than one recurrence. Metastasis occurs in about 30-40% of patients, usually late in the course of the disease. There are no known risk factors (e.g., environmental, dietary, or lifestyle) for chordoma and less than 20 familial cases have been identified around the world.

Statistics

One in one million people get chordoma – a total of about 300 people per year worldwide.

Chordomas are malignant and potentially life threatening tumors.

Currently the median survival in the United States is about 7 years.

The overall survival rates are 68% at 5 years and up to 57% at 10 years.

Complete surgical resection and radiation offer the best chance for long-term survival. Radical resection and high doses of radiation are usually required, sometimes resulting in damage to cranial or sinal nerves. Reconstructive surgery such as bone grafts, tissue grafts, and metal implants is typically needed.

There are currently no approved systemic therapies for chordoma, and only a few clinical trials are available for which chordoma patients are eligible. Off-label treatments are given when possible, but coverage by insurance providers and health systems can be difficult to obtain.

Survey Results

A large scale survey was done to identify the symptoms and challenges of living with chordoma. Information was gathered from both patients and caregivers.

Patient Categories:

40% are skull based chordomas.

Symptoms include: double vision, depression and chronic sinus problems.

31% are sacral chordomas.

Symptoms include: difficulty sitting, difficulty walking and chronic pain

27% are chordomas in the mobile spine.

Symptoms include: chronic pain, difficulty walking and chronic fatigue

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. 72% of the patients in this survey were age 45 or older.

. Some were on long term disability.

. Some experienced a delayed diagnosis.

. There was confusion and unanswered questions.

Patients and their caregivers experienced loneliness or isolation and grief, all while trying to help the patient cope with what was going on in their lives.

My Experience with my husband, Marty.

Marty was diagnosed with lumbar chordoma in 2008 at age 63. We didn't know it, but his chordoma had started growing in his body like the other patients – when he was a fetus – growing in his mother's womb before he was born. When we are being formed in our mothers, we first have a soft spine called the notochord, before the hard spine forms.

When the hard spine forms, the old soft notochord sloughs off and disappears. In Marty's case, like the other patients, a remnant piece of the notochord got trapped in his new hard spine.

It secretly sat in there all his life until one day when some unknown factor triggered the piece into action, and it began to grow. As it grew, it began to press on nerves that caused his symptoms of extreme back pain and difficulty sitting and lying down. He slept in his recliner because he couldn't lie down flat in bed.

Before this time, Marty was newly retired after working for 41 years at the George Banta Printing Company. He was fit and active – he took a daily 3 mile walk and enjoyed our family, as well as his hobbies of speed boat racing, pleasure boating, camping, hunting, snowmobiling, and working in the garage. He was a proud father of our two sons and grandfather to our grandson.

During the time he was sick, Marty had 3 major surgeries, had to learn to walk again twice, and had many rounds of radiation – all down at the University of Wisconsin Hospital in Madison. He also had additional radiation at St. Elizabeth Hospital in Appleton.

Marty passed away on May 18, 2013, at age 68, after struggling with chordoma for 5-1/2 years.

Even though Marty passed away before there was so much progress and awareness of chordoma, he still was able to make a valuable donation to the work being done by the Chordoma Foundation. He and I had talked about that if it was ever possible to donate some of his tumor tissue for research, he would like to do that. When I got active with the Foundation in 2016, (three years after his passing) I found out that hospitals have to keep some tissue samples from each surgery, so I contacted the UW Hospital and arranged for them to send some of Marty's tumor tissue samples to the Chordoma Foundation. The Foundation now has enough samples from more than 250 patients that they can also share with other researchers who are working on finding a cure for other kinds of rare cancer. I know Marty would have been very proud of his personal contribution to the fight against this terrible disease.

Complications to Finding A Cure

There are many complications to finding a cure for any disease,

But…there are even more complications to finding a cure for a very rare cancer.

Remember – Chordoma affects only one in one million people. Therefore, a lot of money would have to be spent on research and treatment methods for a relatively small number of people –

The medical community and pharmaceutical companies wouldn't get a very big "bang for their buck."

There Are Additional Complications In The Medical Community

The first most serious complication is the ignorance of the medical community. Even among some very well-meaning doctors and other medical personnel, many of them either don't know about chordoma at all, or are aware of it, but have wrong information about it.

An example of this -- is back in 2007, when it was thought that chordoma was not cancer and was benign, NOT malignant.

Unfortunately, that was what happened to Marty when he was diagnosed in 2008. His doctor told us that the chordoma acted like cancer, but was NOT malignant!

It has since been proven that chordoma is definitely a malignant cancer. Yet, even today, that misunderstanding persists in the medical community.

I recently read about a person in Australia who was diagnosed with chordoma by a doctor there who said it wasn't malignant.

The patient later found out that was a mistake, and had to undergo 28 hours of corrective surgery over two days to fix the first surgeon's mistakes.

There Are Also Complications With Insurance Companies

A second major complication is the ignorance and greed of some insurance companies. There are crippling costs for the treatment of chordoma, including travel, hotels, loss of wages, and for medical treatment, testing, and medications.

The insurance companies often deny payment for the much-needed treatment – even though the patient has paid his or her insurance premiums – because the companies want to keep the money to increase their bottom line.

Here are some sample costs for some of the procedures often needed for chordoma patients:

CT Scan - $270 - $5,000

MRI Scan - $400 - $3,500

X-Ray - $100 - $1,000

PET Scan - $4,900 - $6,800

Radiation Therapy - $7,500 - $25,500

Proton Beam Therapy - $30,000 - $120,000

These are for a single treatment, and the range of charges that can be made for the exact same treatment.

Also, medications are costly – There was one medication that Marty was put on for awhile that cost $4,000 per month.

Despite all this -- THE GOOD NEWS IS THAT THERE IS HOPE!

A Major Reason Why There Is Hope Is The Chordoma Foundation --

The Chordoma Foundation was created in 2007 in Durham, North Carolina, partially by Josh Sommer, a 21 year old student at Duke University, who was himself diagnosed with cervical chordoma.

It is a non-profit organization with a vision of people overcoming the disease and maintaining their quality of life.

When Josh was diagnosed, his mother, who happened to be a doctor, said they weren't going to sit back and do nothing –

She said she was going to support him, and they were going to fight against his chordoma. He found a few other people with it, and together they organized the Chordoma Foundation in 2007.

Josh changed his studies and has dedicated his life to helping chordoma patients through the Foundation. He is the Executive Director and Co-Founder of the Foundation.

Over the years, the Foundation has created a global movement of patients, families, doctors, and researchers working together to improve the odds for everyone affected by this disease.

From 2007 to 2022, here is some of the progress that's been made:

In 2007: there was virtually no research being done and no infrastructure to enable it;

There was no movement toward new treatments;

Patients were frequently misdiagnosed and mistreated due to limited clinical awareness;

There was nowhere to turn for support and reliable information;

and there was no way for those affected by chordoma to change the outlook.

Much work was done during the ensuing years.

Here is a review of the Chordoma Foundation's most recent research work in 2021:

5% clinical research with the Cetuximab clinical trial at MD Anderson in Houston;

30% pre-clinical research – testing promising drugs in chordoma cell lines and mouse models;

29% in Brachyury drug discovery projects;

6% in enabling resources including tumor tissue/cell lines and mouse models/and data;

and 31% in target discovery, including multi-omics/immune biology projects.

There was $2.5M invested in research in 2021;

14 currently funded research teams;

and 9 new research publications.

In 2021 the Foundation supported three complementary multi-omics projects involving teams at New York University, the University of Minnesota, and Germany's National Center for Tumor Diseases. They're seeking to identify new therapeutic targets, uncover drivers of metastases, and determine whether there are relevant differences between tumors of various anatomic locations.

Dr. Stefan Frohling of the National Center for Tumor Diseases, Germany, says, "What's needed is a comprehensive view into the biology of chordoma tumors and how they vary across patients, and that's what we're aiming to generate. Our vision is to be able to tailor treatment approaches to the unique profile of each patient's tumor."

Encouraging progress continued in multiple labs toward the first drugs that strike at brachyury, the main Achilles' heel of chordoma. Notably, Foundation grantees at the Universty of North Carolina, Oxford University, and The Institute of Cancer Research, London, generated compounds that bind to brachyury an order of magnitude more potently than any previous compounds, including some that appear to suppress the brachyury protein in cells. They also initiated two projects applying powerful computational modeling approaches to further improve the potency of these compounds

The next step is to create compounds that can eliminate brachyury in mouse models and serve as a starting point for brachyury drug discovery programs within companies.

The Drug Screening Program funded a clinical trial at the University of Texas MD Anderson Cancer Center, continued searching for additional options by testing a record 25 treatment concepts in mice, on behalf of 10 researchers or companies. Several of these concepts dramatically decreased tumor growth and have strong potential to move into clinical trials.

A newer area of chordoma research is pediatric chordoma. Even though it appears that the majority of chordoma patients are adults, there are also many pediatric patients, ranging in age from toddlers through young adults. The researchers are working to better understand pediatric chordoma's unique biology and to determine the best treatment approaches for children.

The final major accomplishment of 2021 was the launch of the first lab 100% dedicated to chordoma research. It vastly increases the breadth of experimental capabilities they can offer to the global research community.

<u>Here's where we are today in 2022:</u>

With Research – there is a vibrant global research ecosystem; $15.8M+ spent in cumulative research investments, plus $20M leveraged from others; there are 300+ researchers collaborating toward a cure; there are 30+ high-quality cell and mouse models easily available to scientists; tumor tissue from 250+ patients is banked for

research; and 25+ disease drivers and therapeutic targets have been revealed.

Regarding Treatments – there is a fast-moving therapeutic development pipeline; 6000 drugs have been screened against chordoma cell lines; 70+ promising drugs and combinations have been tested in mice through the Foundation's Drug Screening Program; and seven treatments were brought into clinical trials.

Regarding diagnosis – The Chordoma Foundation created evidence-based guidelines for medical professionals diagnosing and treating chordoma. They have established an approved Doctor Directory which currently lists 215+ experienced doctors.

Regarding support – The Foundation offers comprehensive educational resources for patients and caregivers. There are numerous opportunities for people affected by chordoma to connect with peers. Part of my volunteer work with the Foundation is to serve as a Peer Guide – someone for patients or caregivers to talk to and share concerns with or just to vent to someone who has been in a similar situation. In addition, the Foundation has held International and regional conferences in places such as Boston, the Mayo Clinic in Rochester, MN; at the MD Anderson Hospital in Houston; at Northwestern University in Chicago; at the Langone Health Center in New York City; Italy; and in The Netherlands. I've been fortunate to be able to attend the ones in the United States, including the most recent one on October 1 in New York City.

The Foundation has also created a website called “Chordoma Connections” where people are able to communicate privately with other patients and caregivers, so they can learn from each other and share their concerns. I am honored to be one of the Moderators for them.

Patients, family, and friends do all kinds of fundraising, such as holding 5K and marathon runs, golf outings, bowling events, dinners and dances, and designating birthday pledges to the Foundation. I enjoyed participating in a 5K fundraiser held in Jersey City, in conjunction with the NYC International Conference. All of this support is vital to the Foundation.

Opportunities to influence the future for chordoma patients – There are multiple ways to participate in research from donating tumor tissue to joining a natural history study or clinical trial. Financial donations of all sizes can directly advance research and improve patient care.

<u>Solvable</u>

The Foundation says the great news is that……

“Chordoma is a solvable problem.

It’s not a matter of if, but when.

The key variable is who joins with us to be a part of the solution.”

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You will now be able to help in this effort simply by:

. being aware of this rare cancer;

. being more informed when many of you have the opportunity to vote, and you've heard the politicians talk about health care costs and the need for transparency in those costs; and

. you may know and encourage someone in a health career whom might help find the cure or a treatment for chordoma one day;

I thank you all for your attention and participation today…….

And remember…….. THERE IS HOPE FOR PEOPLE LIVING WITH CHORDOMA!

Are there any questions?